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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/834,926	04/16/2001	Peter Pochlauer	2001_0331A	5439

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EXAMINER

ZUCKER, PAUL A

ART UNIT	PAPER NUMBER
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1621

DATE MAILED: 11/03/2003

15

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/834,926

Applicant(s)

POCHLAUER ET AL.

Examiner

Paul A. Zucker

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on 19 August 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 11-14, 16-19 and 21-23 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 16 and 17 is/are allowed.
- 6) ☒ Claim(s) 11-14, 18, 19 and 21-23 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

Current Status

1. This action is responsive to Applicants' amendment of 19 August 2003 in Paper No 14.
2. Receipt and entry of Applicants' amendment is acknowledged.
3. Applicant's cancellation of claims 15 and 20 is acknowledged.
4. Claims 11-14, 16-19 and 21-23 are pending.
5. The objection to the claims set forth in paragraph 7 of the previous Office Action in Paper No 13 is withdrawn in response to Applicant's amendment.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

6. Claims 21 and 22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 21 and 22 depend upon the canceled claim 20. Claims 21 and 22 are therefore rendered indefinite.

Claim Rejections - 35 USC § 103

7. Claims 11-14, 18, 19 and 23 are finally rejected under 35 U.S.C. 103(a) as being unpatentable over Collet et al (Bulletin de la Société Chimique de France 1973, 12, Pt. 2, pages 3330-3334, English translation, pages 1-18) in view of Effenberger et al

(US 4,859,784 08-1989). NOTE: for the purposes of this rejection claims 18 and 19 are considered to depend from claim 11.

Instantly claimed is a process for the purification of (R) and (S) - α -hydroxycarboxylic acids which consists essentially of recrystallizing impure acids in a hydrocarbon solvent optionally in the presence of a co-solvent. The source of the hydroxycarboxylic acid, as claimed, is an enzyme-catalyzed addition of cyanide ion.

Collet teaches (Translation, page 15, lines 1-11 and page 16, lines 6-11) the production of each antipode of o-bromo and o-chloro mandelic acid in optically pure form (100% ee) via the decomposition of the ephedrine salts and recrystallization of the resulting hydroxy acids from benzene. Collett teaches (Translation, page 15, lines 7-11), for example, that the rotation of the (+)-o-chloromandelic acid can be improved from an initial value of $+57^{\circ}$ to a value of $+159^{\circ}$ for the optically pure (100% ee) material by recrystallization from benzene. The recrystallization also removes any trace of the ephedrine salt resulting in an increase in chemical as well as optical purity.

The difference between the instantly claimed process and that taught by Collet is that Collet teaches (Translation, page 11, line 24- page 12, line 14) producing the mandelic acids by the hydrocyanation of the corresponding benzaldehydes in the presence of acid followed by resolution while in the instant case an enzyme catalyzed process is employed. (NOTE; Collett also teaches use of benzene as a recrystallization solvent to increase the chemical purity of the racemic hydroxy acids)

Effenberger, however, teaches (Column 1, line 66- Column 3, line 11) a method for the synthesis of optically active cyanohydrins via the reaction of an aromatic aldehyde with hydrocyanic acid in the presence of the enzyme D-oxynitrilase as a catalyst. Effenberger teaches (Column 2, lines 52-65) the use the use of a large variety of solvents and their mixtures. Aromatic hydrocarbons (Column 2, lines 52-56) are taught as solvent and the presaturation with water or an aqueous buffer corresponding to the instant co-solvent is also taught (Column 2, line 66- column 3, line 7). Effenberger further teaches (Column 2, lines 52-65) the use of t-butyl methyl ether as a reaction solvent. The amount of water in the water-saturated aromatic solvent is considered to fall within the limits of instant claim 19. Effenberger specifically teaches (Column 2, line 16) the use of o-chlorobenzaldehyde in the process. This corresponds to the intermediate required for synthesis of 2-chloromandelic acid (cf. instant claim 14). Effenberger exemplifies (Column 3, line 49 – column 4, line 54) the cases of benzaldehyde, o- and m -methoxybenzaldehyde which proceed with diastereomeric excesses of 99.3, 90 and 98%, respectively, for the crude product cyanohydrins. Effenberger is silent with regard to the process for conversion of the product cyanohydrins into optically active 2-hydroxycarboxylic acids but does specifically suggest (Column 3, lines 15-19) that the crude solutions of cyanohydrins can be directly converted into optically active 2-hydroxycarboxylic acids:

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"It is not necessary that the crude solutions be purified or treated any further, but can be directly used in further processes under certain conditions, for instance by hydrolysis into the corresponding optically active 2-hydroxycarboxylic acids."

Since aromatic hydrocarbons are taught as solvents the instantly claimed direct recrystallization is obvious in light of Collett's teaching.

It would have been obvious to substitute the improved method for the enzyme-catalyzed production of mandelic acids of Effenberger for the classical hydrocyanation of Collet. The motivation would have been to use the method of Effenberger to produce optically enriched 2-hydroxycarboxylic acids that are the required starting materials for the process of Collett. The motivation would have been to overcome the need, in Collett's process, for a resolution step. By employing the process of Effenberger, the production of the undesired antipode, and the attendant waste of resources, could largely be avoided. Since all references are drawn to the production of the same ultimate products and specifically teach the necessary elements there would have been a reasonable expectation for success. The instantly claimed process would therefore have been obvious to one of ordinary skill in the art.

Examiner's Response to Arguments with Regard to This Rejection

8. Applicants have presented several arguments with regard to this rejection. The Examiner responds to these below:

- a. Applicants argue that no ee value is disclosed by Collett. The Examiner disagrees. Collett discloses optically pure mandelic acids and although the specific terminology "ee" is not employed by Collett, a disclosure of optically pure material is equivalent to a disclosure of 100% ee for that material.
- b. Applicants argue that the numbers for the optical rotations cannot be compared because they were acquired under different conditions. The Examiner disagrees. Applicants have not indicated where these data are to be found in Collett. The Examiner points to Collett (Translation, page 15, 1st paragraph) where the rotations are measured under the same conditions except for concentration (which are given).
- c. Applicants further present arguments directed toward the co-solvent. The Examiner notes that the instantly rejected claims only optionally employ a co-solvent. The nature of the co-solvent is therefore not considered to be a required limitation of the instantly rejected claims.
- d. Applicants further argue that recrystallization from the hydrolysis solvent is not performed and is in fact known in the art. The Examiner agrees but points out that there is therefore nothing patentable in this limitation.

Allowable Subject Matter

9. Claims 16 and 17 are allowed. The following is a statement of reasons for the indication of allowable subject matter: The closest prior art of record: Collet et al (Bulletin de la Société Chimique de France 1973, 12, Pt. 2, pages 3330-3334, English translation, pages 1-18) and Effenberger et al (US 4,859,784 08-1989),

neither alone nor in combination teach or fairly suggest extracting the a crude cyanohydrin hydrolysis reaction mixture with the recrystallization solvent and directly recrystallizing the carboxylic acid therefrom. Claims 16 and 17 are therefore patentable over Collet and Effenberger.

Conclusion

10. Claims 11-14, 16-19 and 21-23 are pending. Claims 11-14 18, 19 and 21-23 are rejected. Claims 16 and 17 are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Paul A. Zucker whose telephone number is 703-306-0512. The examiner can normally be reached on Monday-Friday 7:00-3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann R. Richter can be reached on 703-308-4532. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

Paul A. Zucker, Ph.D.
Patent Examiner
Technology Center 1600

A handwritten signature in black ink, appearing to read "Johann Richter", is written over a horizontal line.

Johann Richter, Ph.D., Esq.
Supervisory Patent Examiner
Technology Center 1600